

**ABSTRACT**

A spectroscopic technique for high-sensitivity, label free DNA quantification uses a shift in an optical resonance (whispering gallery mode, WGM) excited in a 5 micron-sized optical cavity (e.g., a silica sphere) to detect and measure nucleic acids. The surface of the silica sphere is chemically modified with oligonucleotides. Hybridization to the target DNA leads to a red-shift of the optical resonance wavelength. The sensitivity of this 10 resonance technique is higher than most optical single-pass devices such as surface plasmon resonance biosensors. Each microsphere can be identified by its unique resonance wavelength. Specific, multiplexed DNA detection may be provided by using two or more microspheres. The multiplexed 15 signal from two or more microspheres illustrates that a single nucleotide mismatch in an 11-mer oligonucleotide can be discriminated with a high signal-to-noise of 54. This all-photonic WGM biosensor can be integrated on a chip, such as a semiconductor chip, which makes it an easy to 20 manufacture, analytic component for a portable, robust lab-on-a-chip device.